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Cervicothoracic Spinal Manipulation, Autonomic and Psychological Response, and Pain-Mediated Quality of Life in Chronic Neck Pain with Forward Shoulder Posture: A Biopsychosocial Mechanism Analysis from a Randomized Controlled Trial

Ashish Tyagi[1], Dr Tabish Fahim[2], Shubham Tyagi[3], Md Furquan[4], Dr Manish Kumar[5], Babina Rani[6]

[1] PhD scholar, School of Health and Allied Sciences (SOHAS), GD Goenka University, Sohna, Gurugram, India.
bkashutyagi08@gmail.com, Orcid Id: 0009-0005-6167-4169
[2] Associate Professor, School of Health and Allied Sciences (SOHAS), GD Goenka University, Sohna, Gurugram, India.
drtabishfahim4u@gmail.com, Orcid Id: 0000-0001-8480-2593
[3] Physiotherapy consultant, max recovery clinic, sector 22A, pocket C Gurgaon
shubhamtyagi9953@gmail.com ORCID iD: 0009-0000-1912-298
[4] Master's student, Centre for Physiotherapy and Rehabilitation Sciences, Jamia Millia Islamia, New Delhi-110025.
furquanobaid@gmail.com, Orcid Id: 0009-0000-7309-8713
[5] Ex associate professor, physiotherapy department, sohas, GD Goenka university.
mkumar.physio@gmail.com,
Orcid Id: 0000-0001-9181-2319
[6] Physiotherapy Section, Department of Physical Rehabilitation and Medicine, Post Graduate Institute of Medical Education and
Research, Chandigarh, India. says2babina@gmail.com, Orcid Id: 0000-0001-9107-5187
Corresponding author: Dr Tabish Fahim, drtabishfahim4u@gmail.com

ABSTRACT:

Background: Forward shoulder posture in chronic neck pain is associated with autonomic dysregulation, perceived stress, and reduced quality of life, yet randomized evidence on biopsychosocial mechanism is limited.

Purpose: To characterize the autonomic, psychological, and quality-of-life response to adding cervicothoracic spinal manipulation to structured physiotherapy, and to test pre-specified mediation linking the intervention to behavioral-medicine outcomes.

Methods: This assessor-blinded randomized trial allocated 55 adults to manipulation plus physiotherapy (n = 27) or physiotherapy alone (n = 28). Heart rate variability (HRV), Perceived Stress Scale (PSS-10), and WHOQOL-BREF were measured at baseline, 4 weeks, and 8 weeks. Pre-specified mediation tested whether 4-week pain reduction mediated the 8-week effect on physical quality of life; a post-hoc chest-expansion-to-pain path is reported transparently.

Results: Six of eight HRV markers showed significant Group x Time interactions, with

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a transient parasympathetic boost at 4 weeks (RMSSD 32 to 42 ms) that did not persist at 8 weeks (declined to 28 ms). PSS-10 reduction was large (d = -0.97); WHOQOL-Physical, Social, and Environment improved (d = 0.71, 0.49, 0.64). Pre-specified mediation: pain reduction mediated 67.9% of the effect on physical quality of life (indirect 1.997, 95% confidence interval 0.881 to 3.410). Post-hoc exploratory mediation: chest expansion mediated 43.1% of the effect on pain (indirect -0.865, 95% confidence interval -1.769 to -0.138).

Conclusions: Manipulation produced a transient autonomic response (not a durable HRV shift), large stress reduction, and quality-of-life gains driven by pain reduction. Findings are hypothesis-generating and require replication.

INTRODUCTION

Chronic neck pain with forward shoulder posture extends beyond a localized musculoskeletal problem into autonomic, psychological, and quality-of-life domains that the biopsychosocial model of health treats as interdependent rather than separate. Forward shoulder posture is associated with reduced parasympathetic tone, elevated perceived stress, and diminished quality of life across daily activities, work, and social participation [1-4]. These associations are robust descriptively but the causal architecture connecting a clinical intervention to downstream behavioral-medicine outcomes remains under-tested in randomized designs.

Cervicothoracic spinal manipulation is one candidate experimental probe for that architecture. Manual contact at the cervicothoracic junction influences afferent input from cervical paraspinal mechanoreceptors and from the sympathetic chain that traverses this region, with plausible projections to brainstem cardiovascular control nuclei [5-8]. Reviews of manipulation and autonomic outcomes have reported short-term shifts in heart rate variability after thoracic and cervical thrust techniques, although the durability of those shifts has been disputed and a recent meta-analysis reported no sustained between-group HRV difference in chronic spinal-pain populations [9,10]. Taken together, the literature suggests an acute, possibly transient autonomic response rather than a durable shift in autonomic tone.

Psychological stress and quality of life sit downstream of both pain and the autonomic system, and prior trials of manual therapy have reported modest improvements in perceived stress and in physical quality of life [11-13]. What remains unclear is whether those gains are mediated by pain reduction, by autonomic modulation, by direct psychosocial mechanisms attached to the therapeutic encounter, or by a combination of these pathways. Mediation testing in randomized trials is the natural tool for separating these alternatives, but mediation analyses are often added post-hoc and reported without their pre-specification status, which limits inferential strength [14].

The present paper analyses the behavioral-medicine outcome family of a randomized controlled trial of cervicothoracic spinal manipulation added to structured physiotherapy in chronic neck pain with forward shoulder posture. Pain, disability, and posture outcomes are reported in a companion manuscript under submission [15], and pulmonary function and chest-expansion outcomes in a second companion manuscript [16]; this paper covers the autonomic (heart rate variability), psychological (perceived stress, WHOQOL-Psychological), and quality-of-life (WHOQOL-Physical, Social, Environment) outcome family. Two mediation pathways are reported with their pre-specification status explicitly labeled. We frame the manipulation as the experimental probe and the response pattern across autonomic, psychological, and quality-of-life domains as the substantive behavioral-medicine question.

METHODS

Study design

This was a two-arm, parallel-group, assessor-blinded randomized controlled trial conducted at a tertiary-care physiotherapy department in India [details blinded for review], and is reported in line with the CONSORT 2010 statement [17]. The full trial protocol — including allocation procedures, sample-size justification, and intervention parameters — is described in detail in the companion manuscripts that report the pain, disability, and posture outcomes [15] and the pulmonary function and chest-expansion outcomes [16]; key elements are summarized briefly here. Ethics approval was granted by the institutional ethics

committee [details blinded for review]. A computer-generated 1:1 allocation sequence and sequentially numbered opaque sealed envelopes preserved allocation concealment. Allocation was concealed from the assessor for all outcome measurements. All participants provided written informed consent.

Participants

Adults aged 18 to 50 years with chronic neck pain lasting at least 3 months, a Numeric Pain Rating Scale (NPRS) score of at least 3, and forward shoulder posture (bilateral acromion-to-wall distance >= 13 cm) were screened at the study site, as previously described [15]. Exclusion criteria included prior spinal surgery, major trauma, pregnancy, recent manipulation or postural rehabilitation, medication affecting the autonomic nervous system, and major chronic-pain or psychiatric confounders. Body mass index was constrained to 18.5-25 kg/m^2 to limit confounding of HRV and pulmonary outcomes. Seventy-six individuals were screened; 21 were excluded, leaving 55 randomized participants (27 manipulation plus physiotherapy, 28 physiotherapy alone). All 55 completed every treatment session and follow-up assessment, yielding complete data at all three timepoints (Figure 1).

Interventions

The experimental group received cervicothoracic high-velocity, low-amplitude thrust manipulation directed to the lower cervical and upper thoracic regions in addition to a structured physiotherapy program; the comparator group received the identical supervised physiotherapy program without manipulation, as previously described [15,16]. Both groups attended three sessions per week for 4 weeks. The shared physiotherapy program included moist heat, transcutaneous electrical nerve stimulation, myofascial release to the cervical and upper-thoracic musculature, pectoral stretching, chin-tuck exercises, and progressive scapular retraction exercises. No breathing exercises and no autonomic-targeted training (e.g., paced breathing, heart-rate-variability biofeedback) were included in either protocol. This omission is mechanistically relevant: any between-group autonomic or psychological-stress signal cannot be attributed to direct autonomic conditioning.

Outcome measures

The present paper focuses on autonomic, psychological, and quality-of-life outcomes. Pain, disability, posture, pulmonary function, and chest-expansion outcomes are reported in companion manuscripts [15,16] and are not reanalyzed here.

Heart rate variability was assessed using 5-minute resting electrocardiogram (ECG) recordings obtained with a Bio BT (Bluetooth v5) device. Participants rested supine for 5-10 minutes in a quiet, temperature-controlled room before recording, and all recordings were obtained between 10:00 and 11:00 AM to control for diurnal variation in autonomic tone [18,19]. Eight HRV metrics were extracted: time-domain (RMSSD, SDNN, pNN50), frequency-domain (LF, HF, LF/HF ratio), and non-linear Poincare metrics (SD1, SD2). Frequency-domain and time-domain variables were natural-log transformed prior to analysis because of severe right skewness characteristic of HRV data, and group means are reported as geometric means [20]. HRV analysis followed the Task Force guidelines [18].

Perceived stress was measured with the Perceived Stress Scale (PSS-10), a 10-item validated self-report instrument with strong internal consistency in diverse populations [21]. Health-related quality of life was measured with the WHOQOL-BREF (Physical Health, Psychological Well-being, Social Relationships, Environmental Factors) [22]. Raw domain sums were used in analysis to preserve the ordinal structure of the data. The Pain Numeric Rating Scale was retained in this paper only as the mediator in the pre-specified pain -> quality-of-life mediation model; the substantive pain results are reported in the companion manuscript [15].

All outcomes were collected at baseline (T0), 4 weeks (T1), and 8 weeks (T2) by the same blinded assessor.

Statistical analysis

Group x Time effects on each outcome were estimated with linear mixed models with restricted maximum likelihood estimation, with random intercepts for participants and the Group x Timepoint interaction as the parameter of primary interest, as previously described [15]. Repeated-measures ANOVA was used as a planned sensitivity check. Effect sizes are reported as partial eta squared for interactions and Cohen's *d* for 8-week between-group contrasts. Domain-wise Benjamini-Hochberg false-discovery-rate correction was applied within outcome families [23]. To address collinearity among HRV markers, a planned principal component analysis on six log-transformed HRV variables (ln-RMSSD, ln-SDNN, ln-LF, ln-HF, ln-SD1, ln-SD2) was conducted as a sensitivity check [20].

Mediation analysis followed the Baron and Kenny causal-steps framework with bootstrap confidence intervals (5,000 iterations) [24,25]. The temporal structure (mediator at 4 weeks, outcome at 8 weeks) was designed to satisfy the temporal-precedence requirement for mediation. Two paths are reported with their pre-specification status explicitly labeled.

Pre-specified path: Manipulation -> NPRS Reduction (4 weeks) -> WHOQOL-Physical (8 weeks). This path was pre-specified in the trial's analysis plan as a test of whether pain reduction is the mechanism through which the intervention improves physical quality of life.

Post-hoc exploratory path: Manipulation -> Chest Expansion at xiphoid level (4 weeks) -> NPRS Reduction (8 weeks). This path was tested post-hoc and is reported here as hypothesis-generating; replication in a larger sample is required before drawing mechanistic conclusions.

Given the sample size (n = 55), indirect-effect estimates were interpreted cautiously because mediation tests are underpowered in small samples [26]. The reported mediation results cannot definitively distinguish full from partial mediation even where the indirect effect is significant.

RESULTS

Recruitment took place between April and August 2025. Of 76 screened individuals, 55 were randomized and all completed every treatment session and follow-up assessment, yielding complete data at all three timepoints (Figure 1). Baseline autonomic, psychological, and quality-of-life measures were comparable between groups (Table 1). No serious adverse events occurred; mild transient post-treatment soreness was reported by 2 to 3 participants in the manipulation group, resolving within 24 hours.

Heart rate variability outcomes favored manipulation across most metrics (Table 2; Figure 2). Six of eight HRV markers showed significant Group x Time interactions after false-discovery-rate correction: RMSSD ($F(2,106) = 6.01$, $p = .009$, partial eta squared = 0.102), HF power ($F(2,106) = 7.48$, $p = .007$, partial eta squared = 0.124), SD1 ($F(2,106) = 6.01$, $p = .009$, partial eta squared = 0.102), LF/HF ratio ($F(2,106) = 4.27$, $p = .026$, partial eta squared = 0.075), SDNN ($F(2,106) = 4.53$, $p = .026$, partial eta squared = 0.079), and SD2 ($F(2,106) = 3.59$, $p = .041$, partial eta squared = 0.063). pNN50 ($F(2,106) = 2.26$, $p = .126$) and LF power ($F(2,106) = 0.62$, $p = .541$) did not reach significance after correction. Because RMSSD and SD1 are mathematically related (SD1 = RMSSD / sqrt(2)), they yield identical test statistics and represent a single independent finding; the effective number of independent significant HRV findings is therefore five rather than six.

A planned principal component analysis on the six log-transformed HRV variables yielded a first principal component capturing 70.8% of HRV variance and loading on parasympathetic markers; this component showed a significant Group x Time interaction ($F(2,106) = 7.64$, $p < .001$, partial eta squared = 0.126), confirming that the autonomic signal is not an artifact of testing multiple collinear variables.

The temporal pattern of the HRV response was distinctive (Figure 3). The manipulation group showed a sharp parasympathetic increase at 4 weeks (RMSSD geometric mean 32 -> 42 ms) followed by a decline below baseline at 8 weeks (42 -> 28 ms). The comparator group showed a steady, monotonic improvement (32 -> 35 -> 37 ms). An exploratory responder analysis (threshold: 0.5 SD baseline RMSSD = 10.5 ms) found 40.7% of the manipulation group meeting the parasympathetic-responder criterion at 4 weeks and only 3.7% meeting it at 8 weeks (McNemar $p = .002$), with the comparator group showing the opposite pattern (32.1% at 4 weeks; 42.9% at 8 weeks). This pattern is consistent with an acute, transient autonomic response to thrust manipulation that does not persist after treatment cessation, rather than a durable autonomic shift; the finding is hypothesis-generating and the 8-week sub-baseline RMSSD value warrants cautious interpretation given a per-arm n of 27 and the possibility of regression to the mean from elevated 4-week values.

Psychological outcomes favored manipulation for perceived stress but not for the WHOQOL-Psychological domain. PSS-10 showed a strong Group x Time interaction ($F(2,106) = 28.90$, $p < .001$, partial eta squared = 0.353), with the manipulation group reducing perceived stress by 9.1 points (29% reduction) compared with 3.3 points (11%) in the comparator group; the 8-week between-group effect size was large (d = -0.97). The WHOQOL-Psychological domain did not reach significance ($F(2,106) = 2.76$, $p = .068$, partial eta squared = 0.049), although the manipulation group showed numerically greater improvement than the comparator group (change $d = 0.42$). With the trial powered to detect $d >= 0.8$, this result is consistent with insufficient power to detect a moderate effect rather than a true null.

Quality-of-life outcomes favored manipulation across the three remaining WHOQOL-BREF domains (Table 3; Figure 4). Group x Time interactions were significant for the Physical domain ($F(2,106) = 8.83$, $p < .001$, partial eta squared = 0.143; $d = 0.71$), the Social Relationships domain ($F(2,106) = 8.69$, $p < .001$, partial eta squared = 0.141; $d = 0.49$), and the Environmental Factors domain ($F(2,106) = 13.75$, $p < .001$, partial eta squared = 0.206; $d = 0.64$). The Physical domain showed the largest effect, consistent with the pre-specified pain -> quality-of-life mediation finding reported below.

Mediation analyses are reported with their pre-specification status explicitly labeled (Figure 5). The pre-specified path tested whether pain reduction at 4 weeks mediates the manipulation effect on physical quality of life at 8 weeks. The treatment effect on pain at 4 weeks was significant ($a = -2.19$, $p < .001$), and pain at 4 weeks significantly predicted physical quality of life at 8 weeks controlling for treatment ($b = -0.91$, $p = .007$). The indirect effect was significant (1.997, 95% bootstrap confidence interval 0.881 to 3.410), accounting for 67.9% of the total treatment effect on physical quality of life. The direct effect was non-significant after the mediator was included ($c' = 0.94$, $p = .46$). These results are consistent with substantial mediation, although the sample size limits the power to discriminate full from partial mediation [26].

A post-hoc exploratory mediation tested whether xiphoid chest expansion at 4 weeks mediates the manipulation effect on pain at 8 weeks. The a-path was significant ($a = 0.742$, $p < .001$), the b-path was significant ($b = -1.165$, $p = .017$), and the indirect effect was significant (-0.865, 95% bootstrap confidence interval -1.769 to -0.138), accounting for 43.1% of the total treatment effect on pain. The direct effect approached non-significance with the mediator included ($c' = -1.142$, $p = .056$). This path is reported as hypothesis-generating; it was not part of the trial's pre-specified mediation set, and replication in a larger sample is required before drawing mechanistic conclusions about a chest-expansion-to-pain pathway. Three additional pre-specified or exploratory mediations from the trial's analysis plan were either underpowered or null and are summarized in the companion-manuscript reports [15,16]; for completeness, the autonomic-mediator path (RMSSD at 4 weeks -> PSS reduction at 8 weeks) was non-significant ($a = 6.68$, $p = .345$), reflecting the high inter-individual variability in autonomic response.

DISCUSSION

Adding cervicothoracic spinal manipulation to structured physiotherapy produced a coherent biopsychosocial response pattern: a transient autonomic modulation at 4 weeks, a substantial reduction in perceived stress, and improvements in three of four WHOQOL-BREF domains. Pain reduction at 4 weeks substantially mediated the treatment effect on physical quality of life at 8 weeks, identifying pain reduction as a plausible mechanism through which the intervention reaches the behavioral-medicine outcome that matters most to patients. Two interpretive constraints shape the autonomic finding and one interpretive constraint shapes the mediation findings; both are discussed explicitly because their absence would lead to overstated mechanistic conclusions.

The autonomic response should be read as a transient pattern rather than a durable shift. Parasympathetic markers in the manipulation group rose sharply at 4 weeks and declined to or below baseline at 8 weeks, while the comparator group showed gradual monotonic improvement. The exploratory responder analysis (40.7% at 4 weeks, 3.7% at 8 weeks) makes the same point at the participant level. This pattern aligns with a recent meta-analysis of manipulation and HRV that reported no sustained between-group autonomic difference in chronic spinal-pain populations [10] and is consistent with an acute autonomic perturbation that does not persist after the active treatment phase. We are explicit that this finding is hypothesis-generating and **does not** support a claim of durable autonomic remodeling. The 8-week sub-baseline RMSSD finding in the manipulation group warrants particularly cautious interpretation: with a per-arm n of 27, the trajectory — elevation at 4 weeks followed by descent — is most parsimonious with regression to the mean from a transiently elevated baseline, though post-treatment autonomic withdrawal cannot be excluded. The attenuation of the autonomic response between 4 and 8 weeks is consistent with neurophysiological models proposing that spinal manipulation produces a time-limited afferent barrage from mechanoreceptors and proprioceptors at the treated segments, transiently upregulating vagal tone without inducing the sustained synaptic reorganisation required for durable autonomic remodelling [28,29]. In the absence of repeated perturbation or autonomic-targeted adjunct training, this effect is expected to decay within the post-treatment window.

Psychological stress reduction was large and survived false-discovery-rate correction; the WHOQOL-Psychological domain did not reach significance but showed a numerically positive change (a moderate effect size, $d = 0.42$, that may require a larger sample for reliable detection at $n = 55$). The dissociation between large PSS reduction and a non-significant WHOQOL-Psychological signal is not contradictory: PSS-10 captures appraised stress over the past month and has been validated as

sensitive to acute reductions in symptom burden across diverse intervention contexts [21,30], whereas WHOQOL-Psychological samples a broader construct including self-image, body image, and life satisfaction over the previous fortnight that an 8-week mechanical intervention may not reach [22].

The pre-specified pain -> physical quality-of-life mediation result was substantial (67.9% mediated; indirect effect 1.997, bootstrapped 95% CI 0.881-3.410) with a non-significant direct effect when the mediator was included. This pattern is consistent with pain reduction as a primary route through which manipulation reaches physical quality of life in this sample, and aligns with the chronic-pain literature that places pain at the center of QoL change [11,12,31]. The constraint is statistical: with $n = 55$ we cannot discriminate full from partial mediation, and the bootstrapped indirect-effect CI is wide. Replication in adequately powered samples is required before this mediation estimate is interpreted as mechanistically informative. We frame the mediation as substantial but not full and explicitly preserve the possibility that other pathways (autonomic, psychosocial, the therapeutic encounter itself) contribute additively.

The post-hoc chest-expansion-to-pain mediation (43.1% mediated) is reported here for transparency but is hypothesis-generating only. It was not pre-specified, the p value for the b-path is small (0.017) but uncorrected for the multiplicity of post-hoc paths tested in the trial, and the path itself is plausible only if a lower-thoracic mechanical mechanism contributes to pain through chest-wall mobility — a mechanism that the trial cannot confirm at $n = 55$. This path is retained for transparency but is not interpreted as a primary finding.

Three observations situate the findings in the broader biopsychosocial literature. First, the response pattern is multi-domain (autonomic, psychological, quality of life) but the mediation evidence is single-route (pain -> physical QoL); the trial does not support a model in which the autonomic response itself drives the QoL or PSS gains, because the autonomic-to-stress mediation path was non-significant (a = 6.68, $p = .345$). Second, the absence of breathing exercises and autonomic-targeted training in either arm rules out direct autonomic conditioning as an explanation for the HRV response. Third, the pattern fits a model in which manipulation provides an acute neuromechanical perturbation that translates into clinically important pain reduction, which then propagates downstream into quality-of-life domains, while autonomic and psychological response patterns may represent parallel, potentially independent, effects of the intervention.

The clinical implication of these findings is bounded but practically useful: cervicothoracic spinal manipulation, added to structured physiotherapy, can produce a clinically meaningful reduction in perceived stress and an improvement in physical quality of life in chronic neck pain with forward shoulder posture, with the QoL gain operating largely through pain reduction rather than through a durable autonomic shift. The single most important next study is a multi-center, pre-registered trial powered for full-versus-partial mediation discrimination on the pain -> physical QoL pathway, with follow-up extended beyond 8 weeks, ambulatory or task-based autonomic measurement to characterize reactivity rather than only resting tone, and pre-specified testing of all candidate mediation paths including the chest-expansion-to-pain path tested exploratorily here. The contribution of the present trial to the field is to integrate autonomic, psychological, and quality-of-life outcomes from a single manual-therapy randomized comparison and to test mediation paths between them with explicit pre-specification labels — locating cervicothoracic manipulation as an experimental probe into biopsychosocial mechanism rather than as a stand-alone autonomic or psychological intervention.

Limitations

Several limitations should shape interpretation. First, the trial enrolled 55 participants at a single center with a single treating therapist, which limits external generalizability and statistical power for moderation and full-versus-partial mediation discrimination. Second, follow-up ended at 8 weeks; the durability of the pain-mediated quality-of-life pathway beyond 8 weeks is unknown, and the present data should not be used to support claims of long-term behavioral-medicine benefit. Third, the autonomic finding is a transient pattern, **not a claim of durable autonomic remodeling**; the 4-week parasympathetic boost did not persist at 8 weeks, and the sub-baseline RMSSD value at 8 weeks is most parsimoniously explained as regression to the mean from a transiently elevated baseline, with post-treatment autonomic withdrawal as a secondary candidate the present sample cannot exclude. Fourth, the WHOQOL-Psychological domain remained non-significant; the change effect size was a moderate $d = 0.42$ that may require a larger sample for reliable detection. Fifth, the post-hoc chest-expansion-to-pain mediation is exploratory and is reported here only for transparency; it must be replicated in a pre-registered, adequately powered trial before mechanistic conclusions are drawn. Sixth, mediation analysis at $n = 55$ is intrinsically underpowered for full-versus-partial discrimination even where the indirect-effect confidence interval excludes

zero; readers should treat the mediation results as substantial but not definitive [26]. Seventh, ECG-derived HRV in a 5-minute window cannot replace longer recordings or beat-to-beat home monitoring, and the resting-only protocol does not characterize autonomic reactivity to stress.

Future work

Future trials should recruit larger multi-center samples, pre-register all mediation paths including the chest-expansion-to-pain path tested exploratorily here, extend follow-up beyond 8 weeks to characterize durability of the pain-mediated quality-of-life effect, and add ambulatory or task-based autonomic measurements that can characterize reactivity rather than only resting tone. Trials with adequate power for moderation analysis are needed to test the suggestion from the present data that baseline parasympathetic reserve facilitates response to manipulation [27]. Behavioral-medicine outcomes such as patient-reported daily functioning and treatment-related self-efficacy would strengthen interpretation of the quality-of-life pathway.

CONCLUSION

In adults with chronic neck pain and forward shoulder posture, adding cervicothoracic spinal manipulation to structured physiotherapy produced a transient autonomic response pattern at 4 weeks (not a durable autonomic shift), a substantial reduction in perceived stress, and improvements in three WHOQOL-BREF domains. A pre-specified mediation analysis indicated that pain reduction at 4 weeks substantially mediated the manipulation effect on 8-week physical quality of life, with the caveat that $n = 55$ limits full-versus-partial discrimination. A post-hoc exploratory chest-expansion-to-pain mediation is reported transparently as hypothesis-generating only. Findings position cervicothoracic manipulation as an experimental probe into biopsychosocial mechanism rather than as a stand-alone autonomic or psychological intervention, and require replication in adequately powered trials.

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Competing interests declaration

The authors declare that they have no competing interests.

Data availability statement

Deidentified participant-level data and code-derived summary outputs are available from the corresponding author on reasonable request.

AI disclosure

During the preparation of this work the authors used Claude (Anthropic) and Codex (OpenAI) for manuscript drafting, editing, and formatting assistance under human supervision. After using these tools the authors reviewed and edited the content as needed, did not list AI tools as authors, and did not use AI for the generation of data, statistical analyses, or scientific conclusions. The authors take full responsibility for the content of this manuscript.

CRediT authorship contributions

- Author 1: Conceptualization; Methodology; Investigation; Data curation; Formal analysis; Writing - original draft; Writing - review and editing.
- Author 2: Conceptualization; Methodology; Supervision; Writing - review and editing.
- Author 3: Investigation; Writing - review and editing.
- Author 4: Investigation; Data curation; Writing - review and editing.

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TABLES

Table 1. Baseline autonomic, psychological, and quality-of-life characteristics

Characteristic	Manipulation + physiotherapy (*n* = 27)	Physiotherapy alone (*n* = 28)	*p*	SMD
Age, years	34.8 +/- 6.8	36.1 +/- 6.7	.458	-0.20
Female sex, *n* (%)	10 (37.0)	10 (35.7)	1.000	–
BMI, kg/m²	23.3 +/- 1.3	22.7 +/- 1.6	.178	+0.37
NPRS (mediator role only here)	6.4 +/- 1.1	6.8 +/- 1.2	.195	-0.35
PSS-10	31.5 +/- 3.0	30.5 +/- 3.3	.218	+0.34
WHOQOL-Physical	25.1 +/- 3.2	24.8 +/- 3.5	.721	+0.10
WHOQOL-Psychological	24.2 +/- 2.3	24.4 +/- 2.9	.772	-0.08
WHOQOL-Social	12.3 +/- 1.8	12.6 +/- 1.8	.477	-0.19
WHOQOL-Environment	23.8 +/- 2.9	24.0 +/- 3.2	.823	-0.06
RMSSD, ms	37.7 +/- 20.5	38.3 +/- 22.0	.912	-0.03
SDNN, ms	49.8 +/- 18.8	50.7 +/- 20.2	.877	-0.04
pNN50, %	18.4 +/- 15.8	17.7 +/- 15.8	.868	+0.04
LF, ms²	732.0 +/- 627.9	709.1 +/- 627.5	.893	+0.04
HF, ms²	723.4 +/- 679.2	700.2 +/- 683.3	.900	+0.03

Characteristic	Manipulation + physiotherapy (n = 27)	Physiotherapy alone (n = 28)	p	SMD
LF/HF ratio	1.3 +/- 0.7	1.3 +/- 0.7	.950	-0.02
SD1	26.7 +/- 14.5	27.1 +/- 15.5	.911	-0.03
SD2	64.5 +/- 24.3	65.8 +/- 25.4	.854	-0.05

Continuous variables are mean +/- standard deviation. SMD = standardized mean difference. NPRS is included only as a mediator in the pre-specified pain -> physical quality-of-life mediation model; substantive pain results are reported in the companion manuscript.

Table 2. Heart rate variability outcomes (Group x Time interaction effects)

HRV variable	F(2,106)	p (FDR-corrected)	partial eta squared	Interpretation
RMSSD	6.01	.009	0.102	Parasympathetic time-domain
HF (ms^2)	7.48	.007	0.124	Parasympathetic frequency-domain
SD1	6.01	.009	0.102	Mathematically equivalent to RMSSD
LF/HF ratio	4.27	.026	0.075	Sympathovagal balance proxy (interpret cautiously)
SDNN	4.53	.026	0.079	Overall variability
SD2	3.59	.041	0.063	Long-term variability
pNN50	2.26	.126	0.041	Not significant
LF (ms^2)	0.62	.541	0.012	Not significant
PCA: PC1 (parasympathetic, 70.8% variance)	7.64	<.001	0.126	Sensitivity check confirms HRV signal not a collinearity artifact

RMSSD and SD1 are mathematically related (SD1 = RMSSD / sqrt(2)); they yield identical statistics and represent a single independent finding.

Table 3. Psychological and quality-of-life outcomes (Group x Time interaction effects + 8-week Cohen's d)

Outcome	F(2,106)	p (FDR-corrected)	partial eta squared	8-week d	Interpretation
PSS-10	28.90	<.001	0.353	-0.97	Large stress reduction
WHOQOL-Psychological	2.76	.068	0.049	(change d = 0.42)	NS; under-powered for moderate effect
WHOQOL-Physical	8.83	<.001	0.143	0.71	Substantial improvement

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Outcome	F(2,106)	*p* (FDR-corrected)	partial eta squared	8-week *d*	Interpretation
WHOQOL-Social	8.69	<.001	0.141	0.49	Moderate improvement
WHOQOL-Environment	13.75	<.001	0.206	0.64	Substantial improvement
Pre-specified mediation: NPRS (4w) -> WHOQOL-Physical (8w)	–	indirect effect 1.997, 95% CI 0.881 to 3.410	–	67.9% mediated	Substantial mediation; *n* = 55 limits full-vs-partial discrimination
Post-hoc exploratory mediation: CE-xiphoid (4w) -> NPRS (8w)	–	indirect effect -0.865, 95% CI -1.769 to -0.138	–	43.1% mediated	Hypothesis-generating; not pre-specified

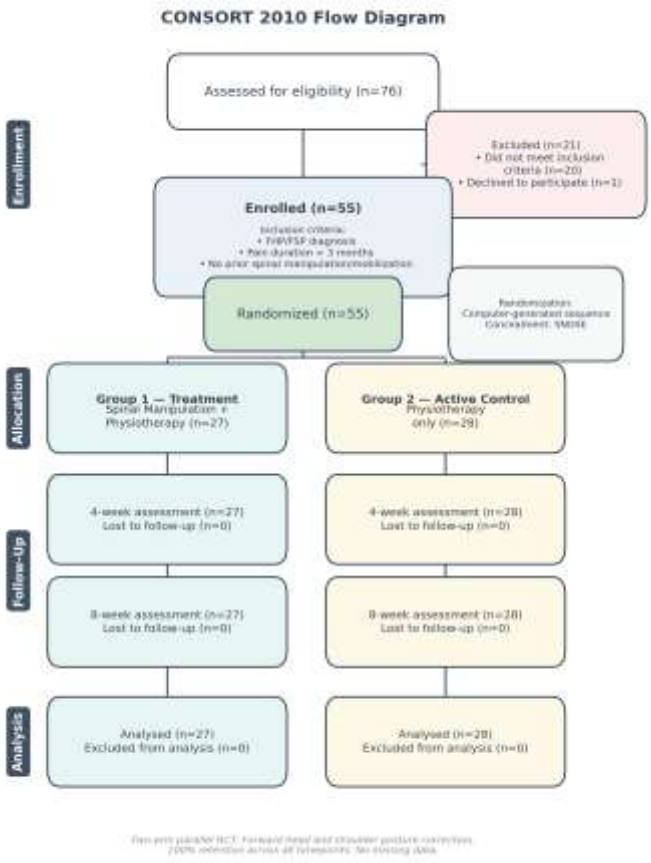

Figure 1. CONSORT 2010 flow diagram showing screening, randomization, treatment allocation, and complete follow-up for all 55 participants.

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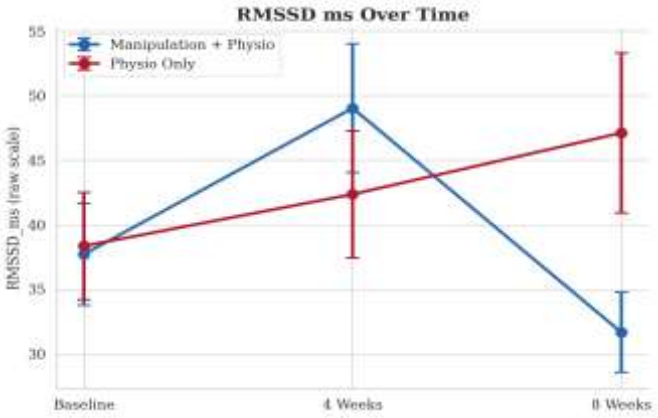

Figure 2. Heart rate variability trajectories for the six markers with significant Group x Time interactions (RMSSD, SDNN, HF, LF/HF, SD1, SD2). Group means with standard errors are shown at baseline, 4 weeks, and 8 weeks.

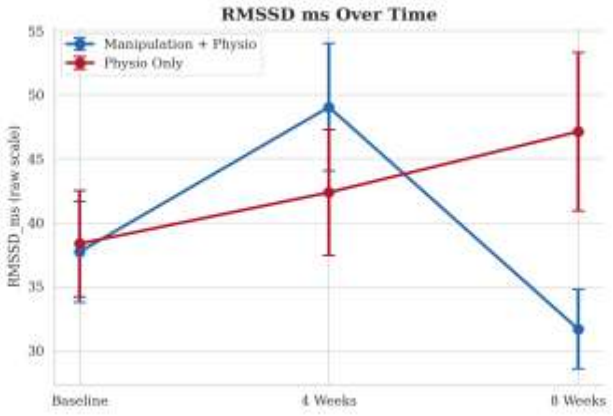

Figure 3. RMSSD temporal pattern by group, showing a transient parasympathetic boost at 4 weeks in the manipulation group followed by decline at 8 weeks; the comparator group shows monotonic improvement. The pattern is hypothesis-generating and does NOT support a claim of durable autonomic remodeling.

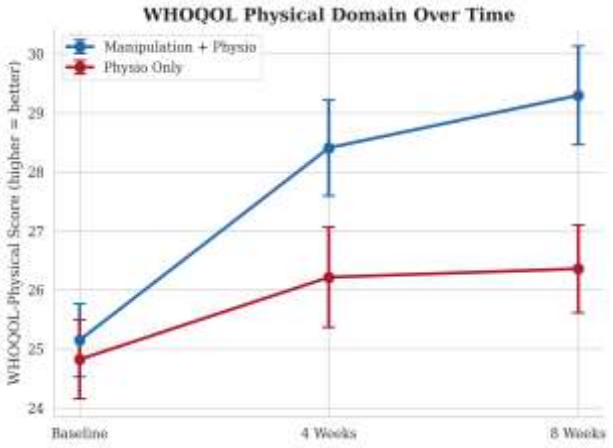

Figure 4. WHOQOL-BREF domain trajectories (Physical, Social, Environment) by group across baseline, 4 weeks, and 8 weeks. The Psychological domain (non-significant) is shown for completeness.

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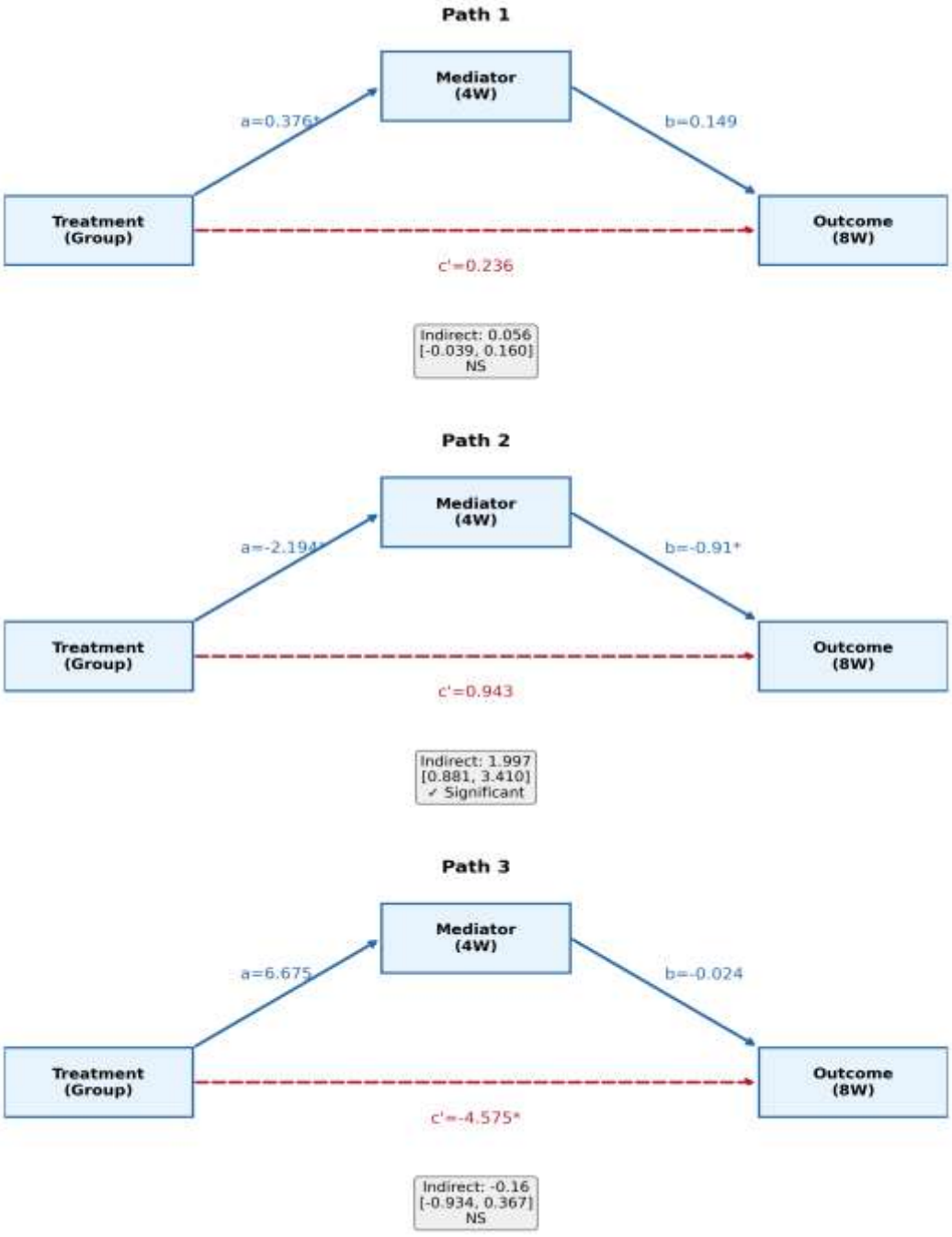

Figure 5. Two-panel mediation diagram. Panel A: pre-specified pain -> physical quality-of-life mediation (67.9% mediated; substantial mediation). Panel B: post-hoc exploratory chest-expansion-to-pain mediation (43.1% mediated; hypothesis-generating only). Pre-specification status is labeled in each panel.